

Intracoronary thrombolysis in evolving myocardial infarction

Sequential angiographic analysis of left ventricular performance

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SUMMARY Since November 1979 left ventricular angiography and coronary arteriography have been performed in 80 patients with evolving acute myocardial infarction in order to attempt coronary recanalisation by local streptokinase infusion. The average delay between the onset of symptoms and streptokinase infusion was 3.6 hours. Thrombolysis was successful in 64% of cases. No serious complications related to the procedure were noted. Of the 12 patients in cardiogenic shock, recanalisation was achieved in only four, of whom two survived.

To evaluate the left ventricular salvage resulting from early recanalisation the last 58 patients had a second left ventricular angiogram and further coronary arteriograms 21 ± 10 days later and 16 patients had a third study three months later. From the left ventricular angiogram in the right anterior oblique projection the ejection fraction and two graphic variables of regional wall motion were computed quantifying the hypokinetic zone. Patients were divided into two groups, according to the patency of the infarct related artery at the second control: group 1 consisted of 28 patients with successful recanalisation confirmed, and group 2 of 30 patients in whom no recanalisation was achieved or secondary reocclusion had occurred. At the second study the ejection fraction was unchanged in group 1 but had significantly decreased in group 2. Regional wall motion improved in group 1 and worsened in group 2, more so in patients without recanalisation than in those in whom secondary reocclusion had occurred. The third study showed a further decrease in ejection fraction in group 2. A progressive decrease in percentage residual stenosis was observed in group 1.

This sequential angiographic study confirms the partial myocardial salvage resulting from early coronary recanalisation during acute myocardial infarction.

Animal experiments have shown that the reperfusion of an obstructed coronary artery within the first six hours of coronary occlusion results in a reduced infarct size.¹⁻³ In man, since the first report by Rentrop *et al.*⁴ four years ago, it has been widely shown that the intracoronary infusion of fibrinolytic drugs can produce coronary artery recanalisation.⁵⁻¹² and this has been proposed as a way of reducing the

extent of acute myocardial infarction. The question, however, of how beneficial the restoration of coronary flow is in the salvage of jeopardised myocardium remains unclear and warrants further investigations.

Eighty patients at the early stage of myocardial infarction were considered for myocardial reperfusion by intracoronary infusion of streptokinase and therefore had left ventricular and coronary angiograms. Fifty eight of these patients had a second haemodynamic and angiographic study three weeks after the intervention to assess the natural history of their left ventricular performance, and 16 had a third

study three months later. Left ventricular function and, in particular, regional wall motion were studied at the chronic stage of infarction in the case of successful and unsuccessful intracoronary thrombolysis to assess the effect of early coronary recanalisation.

Subjects and methods

Beginning in November 1979, patients admitted with an acute myocardial infarction of less than six hours were considered for intracoronary thrombolysis. Diagnostic criteria were typical chest pain lasting more than 30 minutes, which was unresponsive to sublingual glyceryl trinitrate, and ST segment elevation of more than 2 mm in at least two leads in the electrocardiogram, with or without a Q wave. The classical contraindications to streptokinase infusion precluded entry to the trial in only two patients. Informed consent was obtained in all cases.

There were 80 patients (70 men and 10 women) with a mean age of 56 years (range 30-77). The mean delay between the onset of chest pain and admission was two hours and 20 minutes (30 minutes to six hours). Four patients had had a previous myocardial infarction. Twelve patients were in cardiogenic shock.

Procedure

Where possible initial treatment was limited to morphine only for pain. Intravenous glyceryl trinitrate was always avoided. In some cases intravenous atropine, dopamine, or lignocaine were administered. After catheterisation by the femoral route, a right anterior oblique left ventricular angiogram was performed, followed by angiography of only the affected coronary artery in almost every case as determined from the electrocardiogram and left ventricular angiographic data.

Intracoronary thrombolysis was not attempted in nine patients: in two in whom the coronary ostium could not be selectively catheterised; in four of the six patients whose arterial obstruction was incomplete; and in three patients in whom no coronary lesion could be seen on the screen during injections or on video tape replay.

Coronary recanalisation was attempted in the other 71 patients: glyceryl trinitrate, 0.30 mg, was injected into the obstructed coronary artery to rule out spasm. A soft tipped straight metallic guide wire was then inserted into the coronary artery in order to pass the occlusion whenever possible. After an intravenous injection of dexamethasone (8 mg), a bolus of 5000 to 10 000 IU of streptokinase was selectively injected into the occluded artery. Streptokinase was thereafter infused at the rate of 2000 to 4000 IU/min, usually

through the coronary angiography catheter. In 13 cases streptokinase was infused through a 2F radio-opaque catheter advanced through the angiography catheter into the coronary artery to the site of the obstruction. The effect of streptokinase was assessed with an electrocardiogram and coronary opacification every 15 minutes. After successful recanalisation, streptokinase infusion was continued for 15 to 30 minutes longer. If recanalisation was not achieved after 60 minutes, the procedure was usually stopped; in two cases, however, the infusion was continued for a further 30 and 60 minutes.

At the end of the procedure the patients were transferred to the coronary care unit. Treatment consisted of heparin, started when the hourly checked plasma fibrinogen concentration was above 150 mg/100 ml, intravenous glyceryl trinitrate 10 µg/min for 24 hours, nifedipine 30 mg/day orally, and dipyridamole 450 mg/day orally. Antiarrhythmic drugs were used whenever necessary. The patients' progress was followed by continuous electrocardiographic monitoring and a standard electrocardiogram twice a day with MB CK assays every six hours. They were usually discharged after two weeks taking nifedipine, dipyridamole, and oral anticoagulants in all cases.

EVALUATION OF SUCCESS AND PATIENT GROUPS

In the last 58 consecutive patients, a second catheterisation (right anterior oblique left ventricular angiogram and full coronary angiogram) was done 10 to 45 days (mean 21 ± 10 days) after the initial examination. The patients were divided into two groups according to the patency of the initially obstructed artery. Group 1 consisted of 28 patients in whom the coronary artery had been recanalised and was patent at the second study. Group 2 consisted of 30 patients in whom the coronary artery involved was occluded at the second study, either because of secondary reocclusion after an initially successful recanalisation (group 2a, 10 patients), or because the thrombolysis was unsuccessful, or lysis was not attempted (group 2b, 20 patients).

The evolution of myocardial function was studied by comparative analysis of the left ventricular angiograms obtained initially and during the second catheterisation.

In 16 patients (seven from group 1 and nine from group 2) a third identical investigation was done three months later, to study the chronic evolution of the left ventricular function. In these patients, the residual coronary stenosis (percentage diameter narrowing) was measured at each of the three studies.

ANGIOGRAPHIC DATA ANALYSIS

End-systolic and end-diastolic left ventricular volumes (Simpson's rule) and the ejection fraction were

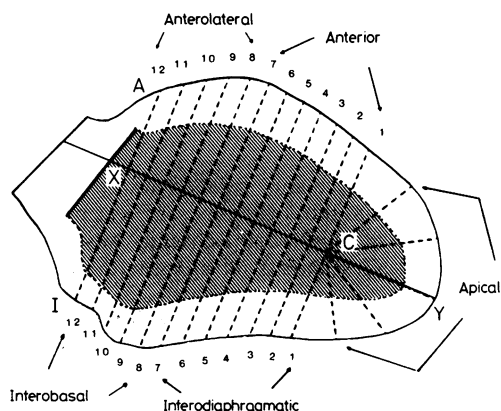


Fig. 1 Regional wall motion. The left ventricular systolic and diastolic outlines were matched according to Leighton's method. Point C is two-thirds of the distance from X to Y on the major axis. Twelve equidistant axes perpendicular to the major axis are drawn from point X to point C to study the wall motion in the following regions: anterolateral (A 12 to A 8), anterior (A 8 to A 1), inferobasal (I 12 to I 7), and inferior (I 7 to I 1). The apex was studied by five radiating axes (15° steps) centred on point C.

computed from each left ventricular angiogram. Regional wall motion was studied from a superposition of systolic and diastolic left ventricular outlines with a correction for apex rotation, according to the method of Leighton *et al.*¹³ The ventricular cavity was divided into 30 segments by 29 axes (Fig. 1). The percentage change in each axis was compared with the theoretically normal values derived from the study of 20 normal subjects and the regional contractility was expressed as a linear graph (Fig. 2) in which the upper and lower limits of normal (mean \pm 2SD) are shown. Hypokinesia was considered when the percentage shortening of an axis was more than 2SD below normal mean. To evaluate the importance of the hypokinetic zone and compare successive angiograms, two indices were computed from the graphic wall motion outline (Fig. 3): the surface limited by the studied patient's curve and the lower limit of normal values was planimetered and this so-called "hypokinetic surface" was expressed in cm^2 . A so-called "hypokinetic length" was defined as the percentage of the total circumference which was considered hypokinetic on the graphic representation. These two variables give an estimation of the importance of the hypokinetic zone, though they obviously cannot be considered as the true physical measure of this zone. Results are given as mean \pm SD.

Statistical analysis was done using Student's *t* test as applied to paired and unpaired data.

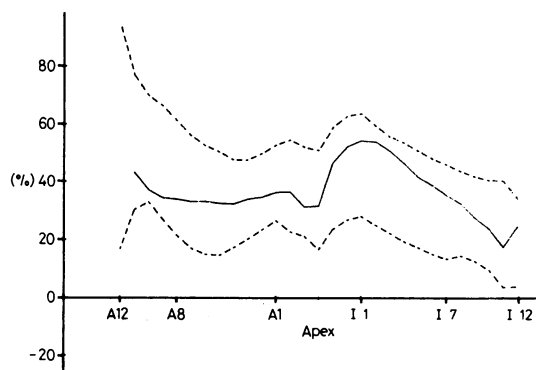


Fig. 2 Normal regional wall motion. On the vertical axis is shown the percentage shortening of the axes; and on the horizontal axis, the number of each axis. A normal wall motion curve (solid line) remains within the limits set by normal mean \pm 2 SD (dashed lines).

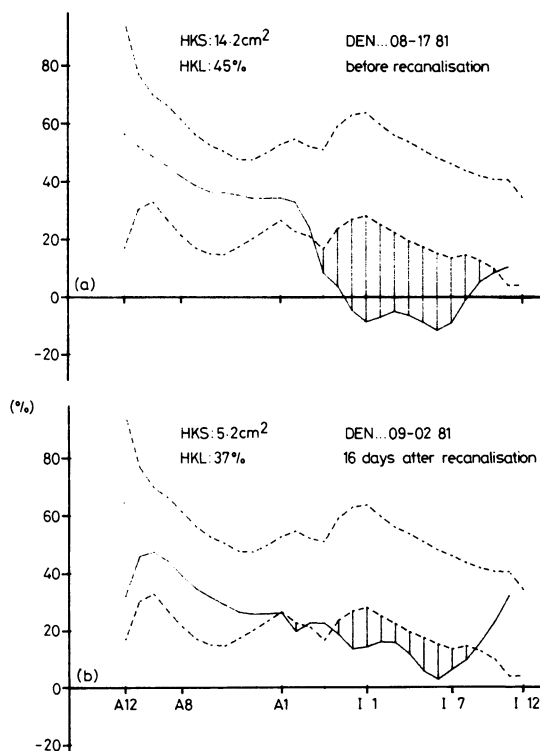


Fig. 3 Wall motion before and 16 days after successful recanalisation of a right coronary artery in a patient with inferior myocardial infarction. Upper panel, before recanalisation, the regional wall motion curve crosses the lower limit of normal and limits with it a "hypokinetic surface" (hatched) which is planimetered (hypokinetic surface (HKS) = 14.2 cm^2). The measured length of the hypokinetic segment (HKL) is 45% of measured total left ventricular circumference.

Lower panel, at the second control, HKS has decreased by 63% to 5.2 cm^2 and HKL by 18% to 37%.

Results

CORONARY ANGIOGRAPHIC DATA

Coronary angiography was performed 3.6 ± 1.2 hours after the onset of chest pain. It showed complete coronary occlusion in all patients except six in whom there was only a severe stenosis (92% of cases). The left coronary artery was affected in 50 patients (left main, 4; left anterior descending, 32; circumflex, 12; diagonal, two) and the right coronary artery in 30 patients. Intracoronary glyceryl trinitrate had no effect except in two cases where it was followed by a transient reopacification of the first centimetres of the artery. The guide wire could be pushed through the obstruction in 32 cases, with a subsequent sluggish and incomplete opacification of the occluded artery, often showing unmistakable evidence of intravascular thrombosis at the occlusion site.

Satisfactory recanalisation was obtained by intracoronary streptokinase in 39 out of 61 (64%) patients whose coronary artery was occluded and in whom the complete procedure was applied. The mean perfusion time was 50 minutes (20-120 minutes) and varied according to the quality of the recanalisation and the patient's clinical status. The mean infused

dose of streptokinase was 180 000 IU (40 000 to 280 000). After recanalisation, a greater than 50% stenosis (visual estimation) was observed at the site of the obstruction in all cases.

CLINICAL COURSE

In cases of successful recanalisation, a striking improvement in the symptoms and electrocardiographic signs of myocardial ischaemia was observed, the elevated ST segments returning to the isoelectric line within a few minutes. Ventricular extrasystoles were frequent during the first few minutes after recanalisation but were easily controlled by intravenous lignocaine. Six patients had ventricular tachycardia which had to be cardioverted.

Of the 12 patients with cardiogenic shock on admission, eight died during the procedure, in two cases despite recanalisation. These patients had left main occlusion in four instances (in two cases recanalisation was attempted during artificial ventilation and heart massage) and a proximal left anterior descending artery occlusion in four cases. Of the 4 other patients with cardiogenic shock, recanalisation was not achieved in two who died within 48 hours after admission; the two other patients in whom recanalisation

Table 1 Individual values of group 1 (successful confirmed recanalisation)

Cases	HR (beats/min)		LVEDP (mmHg)		LVEDV (ml/m ²)		EF (%)		HKS (cm ²)		HKL (%)		Coronary artery
	Base	2nd Ex	Base	2nd Ex	Base	2nd Ex	Base	2nd Ex	Base	2nd Ex	Base	2nd Ex	
1	97	110	15	12	70	88	53	56	20	15	40	31	LCx
2	90	100	8	5	105	78	40	45	10	6	45	29	RCA
3	92	80	16	25	76	100	53	51	11	6	50	30	RCA
4	94	90	25	22	120	125	35	32	18	14	55	57	LAD
5	86	65	25	13	73	79	41	41	10	6	54	45	RCA
6	86	97	18	12	103	110	60	58	10	8	42	45	RCA
7	120	67	15	11	80	84	48	51	9	9	41	38	RCA
8	77	71	8	17	63	110	44	41	10	13	44	44	LAD
9	54	70	15	12	126	138	49	55	14	5	45	37	RCA
10	64	61	25	15	103	96	52	59	18	8	45	43	LAD
11	100	94	18	25	104	99	45	47	9	9	53	53	LAD
12	63	93	12	12	89	92	65	57	11	5	42	36	LCx
13	92	59	20	18	72	91	32	57	22	4	64	16	LAD
14	91	90	20	20	56	86	50	41	11	15	51	48	LAD
15	86	73	20	10	62	97	41	56	20	12	40	39	RCA
16	88	67	15	14	80	89	50	50	7	10	38	44	RCA
17	80	60	20	8	71	106	48	32	14	18	53	60	LAD
18	110	100	40	40	112	132	21	20	—	—	—	—	LAD
19	81	107	15	10	117	89	41	44	23	16	74	61	RCA
20	80	86	15	10	101	93	37	43	24	18	56	46	LAD
21	103	94	25	10	101	80	35	48	16	11	75	45	LAD
22	80	78	16	8	108	67	64	58	3	3	20	28	LAD
23	90	87	14	5	94	93	63	59	5	4	33	30	LCx
24	60	86	14	30	70	87	55	40	12	12	45	50	LAD
25	105	101	35	10	72	68	47	50	6	13	55	47	LAD
26	62	92	10	5	81	91	41	62	8	1	42	6	LAD
27	100	100	22	14	63	72	54	59	8	6	33	36	LAD
28	63	63	20	12	78	98	59	59	1	4	7	31	RCA
Mean	86	84	19	14	88	94	47	49	12	9	46	40	
SD	16	16	7	8	20	17	10	10	6	5	14	13	
p	NS		p<0.02		NS		NS		p<0.01		p<0.05		

LAD, left anterior descending artery; LCx, left circumflex artery; RCA, right coronary artery; EF, ejection fraction; HKL, hypokinetic length; HKS, hypokinetic surface; HR, heart rate; LVEDP, left ventricular end-diastolic pressure; LVEDV, left ventricular end-diastolic volume; Base, before recanalisation; 2nd Ex, second study, 10 to 45 days after recanalisation.

Table 2 Individual values of group 2a (recanalised patients with secondary reocclusion) and group 2b (no recanalisation)

Group	Pts	HR (beats/min)		LVEDP (mmHg)		LVEDV (ml/m ²)		EF(%)		HKS (cm ²)		HKL (%)		Coronary artery
		Base	2nd Ex	Base	2nd Ex	Base	2nd Ex	Base	2nd Ex	Base	2nd Ex	Base	2nd Ex	
2a n=10	1	77	81	15	17	92	105	50	47	9	7	32	37	RCA
	2	97	70	12	10	72	110	45	47	10	14	38	46	RCA
	3	91	71	12	10	65	68	64	51	5	7	26	27	D
	4	70	92	20	20	123	136	50	34	8	16	48	48	RCA
	5	109	72	12	12	74	94	58	47	6	7	30	28	RCA
	6	94	82	20	25	66	86	62	58	1	2	11	22	RCA
	7	60	64	16	8	79	88	46	51	5	11	33	41	LCx
	8	62	73	14	13	60	138	38	32	10	13	47	55	LAD
	9	80	67	6	15	90	107	48	45	13	9	40	56	RCA
	10	91	105	18	8	78	87	57	60	9	6	37	35	RCA
	Mean	83	78	15	14	80	102	52	47	8	9	34	40	
SD	16	13	4	6	18	22	8	9	3	4	11	12		
p	NS		NS		p<0.02		NS		NS		p<0.05			
2b n=20	1	83	117	20	27	132	100	53	30	5	14	26	53	LAD
	2	115	64	8	30	89	135	47	28	6	14	39	53	LAD
	3	59	71	12	10	121	103	72	62	2	3	21	16	LCx
	4	92	74	10	8	73	110	65	56	3	5	15	30	RCA
	5	83	66	10	12	74	98	45	38	18	20	55	62	RCA
	6	85	86	35	30	74	112	38	33	—	—	—	—	LAD
	7	72	78	24	15	82	85	52	50	9	17	32	37	LAD
	8	73	65	15	20	55	75	67	58	4	5	42	47	RCA
	9	71	73	15	10	96	89	57	49	10	16	34	54	LAD
	10	82	92	12	20	74	97	56	49	8	10	32	45	LCx
	11	84	80	12	10	58	93	68	55	9	16	32	29	LCx
	12	107	90	16	12	94	104	53	36	4	13	39	70	LCx
	13	110	94	30	18	74	93	59	29	11	20	53	60	LAD
	14	67	90	15	—	88	126	56	42	3	16	29	38	RCA
	15	58	95	15	25	98	94	61	24	—	—	—	—	LCx
	16	143	82	16	30	85	143	36	28	16	18	53	56	LAD
	17	125	97	25	8	54	60	56	52	6	6	43	38	LCx
	18	64	80	25	25	60	120	47	30	15	12	61	86	RCA
	19	62	71	15	10	129	106	53	51	2	4	36	44	RCA
	20	69	75	—	5	55	67	69	65	1	2	11	18	D
Mean	86	81	18	17	83	101	55	43	7	12	37	46		
SD	23	13	7	9	23	21	10	13	5	6	14	18		
p	NS		NS		p<0.01		p<0.001		p<0.001		p<0.001			
2a+2b n=30	Mean	85	80	17	16	82	101	54	45	7	11	36	44	
	SD	21	13	6	8	21	21	9	12	4	6	13	16	
	p	NS		NS		p<0.001		p<0.001		p<0.001		p<0.001		

D, diagonal artery. Other abbreviations as in Table 1.

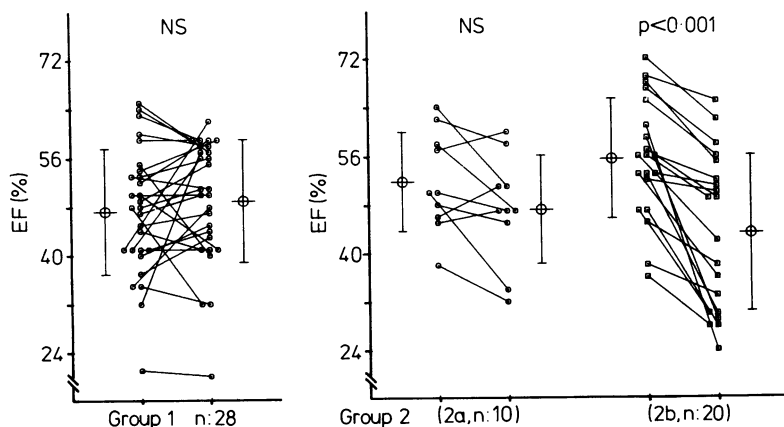


Fig. 4 Ejection fraction before and 15 to 45 days after intracoronary thrombolysis in group 1 on the left (successful confirmed recanalisation) and group 2 on the right (recanalisation with secondary reocclusion (2a), or no recanalisation (2b)).

Ejection fraction does not change in group 1, but significantly worsens in group 2 (more in 2b than 2a).

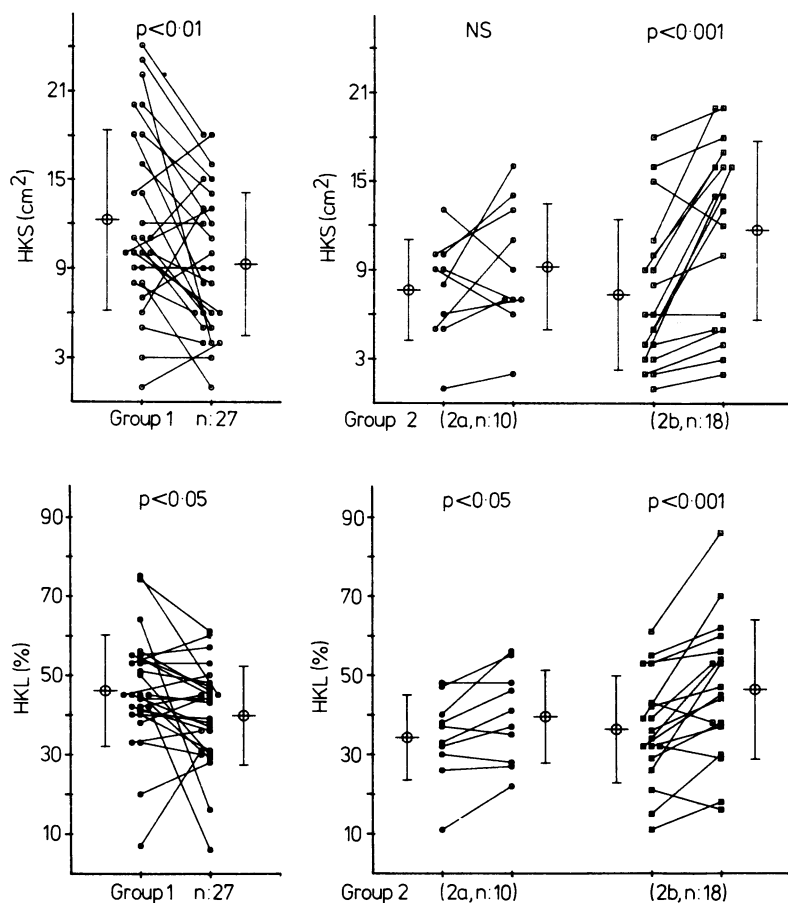


Fig.5 Regional wall motion indices before and 10 to 45 days after the recanalisation attempt. Upper panel, hypokinetic surface; lower panel, hypokinetic length (as % of total left ventricular circumference).

Both variables decrease in group 1 (confirmed successful recanalisation) and increase in group 2 (secondary reocclusion after an initially successful recanalisation (group 2a)) and unsuccessful or no recanalisation (group 2b)).

was successful were alive and without symptoms 12 and 14 months later.

No complication directly related to the recanalisation procedure was noted.

Creatine kinase activity which was normal on admission (<100 IU), increased to 1500 ± 180 IU. Four patients in whom recanalisation was successful complained a few days later of chest pain with increased creatine kinase concentrations and electrocardiographic abnormalities suggesting extension of myocardial infarction. The second angiographic study showed coronary reocclusion in only two cases. There was no extension of myocardial infarction in patients in whom recanalisation was unsuccessful.

None of the 39 patients in whom recanalisation was

successful died during the hospital stay, but two of the 22 patients in whom it was unsuccessful died.

ANGIOGRAPHIC EVALUATION OF LEFT VENTRICULAR PERFORMANCE

Comparison of first and second left ventricular angiograms

Individual data are given in Tables 1 and 2 and in Figs. 4 and 5. In one patient in group 1 and two patients in group 2 regional wall motion was not assessed because of a previous history of myocardial infarction.

Group 1: (successful confirmed recanalisation) 28 patients—There was no difference in the initial values of heart rate: $86 \pm 16/\text{mn}$ v $84 \pm 16/\text{mn}$ (NS), and left ventricular end-diastolic volume 88 ± 20 ml/m² v 94 ± 17 ml/m² (NS). Left ventricular end-diastolic

Table 3 Third study, three months after initial assessment: individual values at each examination of seven patients in group 1 (successful recanalisation) and nine patients in group 2 (secondary reocclusion (2a) or no recanalisation (2b)) who had three haemodynamic studies

Group	Cases	LVEDV (ml/m ²)			EF (%)			HKS (cm ²)			HKL (%)			% S			Coronary artery
1	1	101	80	70	35	48	61	16	11	3	75	47	29	60	60	60	LAD
	2	104	89	111	45	47	36	9	9	15	53	53	59	95	10	10	LAD
	3	72	91	104	32	57	58	22	4	4	64	16	20	90	80	50	RCA
	4	80	89	83	50	50	56	7	10	9	38	44	39	90	50	40	RCA
	5	62	97	79	41	56	46	19	12	16	40	39	46	95	60	45	RCA
	6	117	89	85	41	44	46	23	16	7	74	61	27	70	60	65	RCA
	7	101	93	135	37	43	46	24	18	7	56	46	46	90	70	60	LAD
	Mean	91	91	95	40	49	50	17	11	9	57	44	38	84	56	45	
	SD	20	6	23	6	5	9	7	5	5	15	14	14	14	22	18	
	p	NS NS NS			p<0.05 NS			NS NS NS			NS NS NS			p<0.05 p<0.05 p<0.01			
2a	1	78	87	86	57	60	49	9	6	9	37	35	46	90	100	100	RCA
	2	79	88	93	46	52	56	10	22	10	33	42	31	95	100	100	LCx
	3	59	138	146	38	32	21	10	13	19	47	55	67	95	100	100	LAD
	4	82	85	93	52	50	53	9	17	7	32	37	32	100	100	100	RCA
	5	96	89	119	57	49	39	10	16	10	34	54	56	100	100	100	LAD
	6	74	93	125	59	29	33	11	20	15	53	50	60	100	100	90	LAD
	7	88	126	92	56	42	34	3	16	14	29	38	50	100	100	100	RCA
	8	35	75	87	67	58	45	4	5	7	42	47	48	100	100	100	RCA
	9	94	104	135	53	56	43	4	13	11	39	70	54	100	100	100	LCx
	Mean	76	98	108	54	47	41	8	14	11	38	49	49	—	—	—	
2b	SD	19	21	23	8	11	11	3	6	4	8	12	12	—	—	—	
	p	p<0.05 NS			NS p<0.05			p<0.01 NS			p<0.02 NS			p<0.01			
		p<0.01			p<0.02			NS									

% S, percent diameter narrowing on residual coronary stenosis. See Table 1 for other abbreviations.

pressure was decreased from 19 ± 7 mm Hg to 14 ± 8 mmHg ($p < 0.02$).

The ejection fraction was initially $47 \pm 10\%$ (below 60% in 24 cases) and was unchanged at the second study ($49 \pm 10\%$, NS). The hypokinetic surface decreased from 12 ± 6 cm² to 9 ± 4 cm² ($p < 0.01$) and the hypokinetic length from $46 \pm 14\%$ to $40 \pm 12\%$ ($p < 0.05$). In one out of 15 cases of proximal left anterior descending artery occlusion, a typical left ventricular aneurysm (defined as a protrusion of the akinetic surface out of the normal diastolic contour) was seen at the second study. In this patient there was a six hour delay between the onset of pain and recanalisation.

Group 2 (no recanalisation or reocclusion) 30 patients—The heart rate (85 ± 21 /min *v* 80 ± 13 /min, NS) and left ventricular end-diastolic pressure (17 ± 6 mmHg *v* 16 ± 8 mmHg, NS) remained unchanged. The left ventricular end-diastolic volume increased from 82 ± 21 ml/m² to 101 ± 21 ml/m² ($p < 0.001$). The ejection fraction decreased from $54 \pm 9\%$ to $45 \pm 12\%$ ($p < 0.001$). In eight cases, the initially subnormal ejection fraction was much decreased, below 40%. The hypokinetic surface increased from 7 ± 4 cm² to 11 ± 6 cm² ($p < 0.001$), as did hypokinetic length: $36 \pm 13\%$ to $44 \pm 16\%$ ($p < 0.001$). In this group, five out of the eight patients with proximal left anterior descending occlusion developed a typical left ventricular aneurysm. The angiographic results obtained

in subgroups 2a (secondary reobstruction, 10 patients) and 2b (no recanalisation, 20 patients) are given in Table 2. The ejection fraction decreased less in subgroup 2a ($52 \pm 8\%$ to $47 \pm 9\%$, NS) than in subgroup 2b ($55 \pm 10\%$ to $43 \pm 13\%$, $p < 0.001$). The change in hypokinetic surface was small in subgroup 2a (8 ± 3 cm² to 9 ± 4 cm², NS) and large in subgroup 2b (7 ± 5 cm² to 12 ± 6 cm², $p < 0.001$). Changes in hypokinetic length were similar to those of hypokinetic surface: $34 \pm 11\%$ to $40 \pm 12\%$ ($p < 0.05$) in group 2a, $37 \pm 14\%$ to $46 \pm 18\%$ ($p < 0.01$) in group 2b.

Comparative study of groups 1 and 2

The anatomical distribution of the coronary obstruction in groups 1 and 2 was statistically similar except for the number of left anterior descending artery occlusions (15 in group 1 *v* eight in group 2, $p < 0.05$). Lesions were more often distal in group 2 than in group 1. This explains the fact that initial global or regional left ventricular function alterations were more severe in group 1 than in group 2 as shown by the ejection fraction ($p < 0.01$), hypokinetic surface ($p < 0.001$), and the hypokinetic length ($p < 0.01$).

Influence of delay between onset of pain and beginning of intracoronary thrombolysis

In group 1 the mean delay was 3.3 ± 1.2 hours, while it was 4.6 ± 1 hours in group 2. This difference is significant ($p < 0.02$). No correlation was found, however, between the delay and the percentage change in

left ventricular function variables.

Three months later, a third left ventricular angiogram and coronary angiogram was obtained in 16 of these 58 patients (seven from group 1 and nine from group 2). Results are given in Table 3. No coronary reocclusion was noted in patients in group 1 but there was one patient with spontaneous recanalisation in those in group 2. In the patients in group 1, the percentage residual coronary narrowing decreased from $84 \pm 14\%$ to $56 \pm 22\%$ ($p < 0.05$) at the second study and further decreased to $45 \pm 18\%$ ($p < 0.01$) at the third. Between the second and third studies in group 1, the ejection fraction did not change ($49 \pm 5\%$ v $50 \pm 9\%$, NS) nor did the hypokinetic surface ($11 \pm 5 \text{ cm}^2$ v $9 \pm 5 \text{ cm}^2$, NS) and the hypokinetic length ($44 \pm 14\%$ v $38 \pm 14\%$, NS). In group 2, the ejection fraction further decreased from $47 \pm 11\%$ to $41 \pm 11\%$ ($p < 0.05$) but neither the hypokinetic surface ($14 \pm 6 \text{ cm}^2$ v $11 \pm 4 \text{ cm}^2$, NS) nor the hypokinetic length ($49 \pm 12\%$ v $49 \pm 12\%$, NS) was changed.

Discussion

EFFICACY OF SELECTIVE STREPTOKINASE INFUSION IN CLINICAL ACUTE MYOCARDIAL INFARCTION

In this series of 80 patients who were considered for intracoronary thrombolysis who underwent early coronary angiography, myocardial infarction was found to be the result of coronary obstruction in all but six cases (92%), higher than the figures usually given in the published reports (approximately 80% in American or German studies).^{14,15}

The progressive recanalisation with streptokinase confirmed the thrombotic nature of the occlusion as seen on coronary angiography. The angiographic aspect of the occlusion during recanalisation was also often suggestive of a thrombus. The failure of intracoronary glyceryl trinitrate in our series as well as in others rules out spasm, as opposed to Olivia and Breckenbridge's¹⁶ report.

Our 64% success rate is slightly less than that commonly reported in smaller series, which range from 67% (Reduto *et al.*¹⁰) to 81% (Rutsch *et al.*¹²). Ganz *et al.*⁵ have even reported a 90% success rate, which could be explained by the infusion of streptokinase to the immediate vicinity of the clot using a thin catheter inserted through the lumen of the angiography catheter or by the addition of plasmin to streptokinase (thrombolysin) or both.

After recanalisation, the rapid regression of chest pain and the simultaneous return of the ST segment to the isoelectric line mirror the disappearance of ischaemia in the jeopardised myocardium⁵⁻⁹ rather than an acceleration of the necrotic process as has been suggested,¹⁷ which would not accord with the

Cribier, Berland, Champoud, Moore, Behar, Letac

improvement in regional wall motion after recanalisation.

Myocardial necrosis occurred in every case despite recanalisation, as indicated by the constant appearance of a Q wave on the electrocardiogram and long term persistence of a hypokinetic zone on the left ventricular angiogram. It is probable that only very early recanalisation, probably within 20 to 30 minutes, could totally avoid myocardial infarction, as has been observed when recanalisation was done immediately after an acute obstruction during catheterisation.^{18,19}

In two patients, reobstruction occurred 48 hours after recanalisation at the same site, as was confirmed by a subsequent angiogram. This reocclusion was accompanied by a sharp increase in CK levels, showing that initially an ischaemic zone had been preserved from necrosis by the recanalisation.

COMPLICATIONS

No accident or incident could be related to the initial left ventricular angiogram performed in all patients except in the case of those in cardiogenic shock.

Reperfusion ventricular arrhythmias, premature ventricular beats, or even episodes of ventricular tachycardia should not actually be considered complications of intracoronary thrombolysis since they were not followed by any adverse effect and were often a sign of successful recanalisation.

In our series, intracoronary thrombolysis had little beneficial effect in patients with cardiogenic shock: eight of 12 such patients died during the procedure, in four of these after a successful revascularisation which could suggest a possible aggravating effect of the recanalisation. In two cases, however, long term survival could, at least in part, be attributed to the recanalisation.

The total dose of streptokinase infused did not exceed 280 000 IU in our series, though some authors have used twice that amount.⁷ This could account for the absence of haemorrhagic complications in our series, compared to that reported in a large multicentre study of 7.4%.²⁰

LEFT VENTRICULAR FUNCTION AFTER INTRACORONARY THROMBOLYSIS

The lack of accurate data concerning the natural history of left ventricular function during acute myocardial infarction and the ethical problems involved in randomisation after the initial left ventricular and coronary angiograms make an evaluation of the benefits of recanalisation on myocardial function especially difficult. In other reports, the effects of intracoronary thrombolysis were evaluated by the evolution of the ejection fraction, either immediately or a few weeks later.^{5,6,21,22} Evaluation of regional wall motion was either subjective²² or limited to five

ventricular zones.²¹ The indices of ventricular function we used after a precise localisation of the hypokinetic zone afford a better appraisal of changes in left ventricular performance.

In our study two groups of patients were compared. Group 1 consisted of all patients in whom recanalisation was achieved and in whom it persisted. Group 2, used as a control group, was more heterogeneous. Of its 30 patients, the 20 in whom recanalisation was unsuccessful (including the five who did not even have infusion of streptokinase) can be considered as real control subjects, while the validity of using as control subjects the 10 patients whose coronary artery reoccluded could be questioned.

Changes in ejection fraction after intracoronary thrombolysis are difficult to assess. During the acute phase of myocardial infarction there is a compensatory hypercontractility of the intact myocardium probably related to increased plasma catecholamines.²³ This effect could be amplified by afterload reduction with infusion of glyceryl trinitrate,¹¹ which was avoided in this study. Therefore the stability of the ejection fraction in group 1 should not be construed as a lack of improvement in left ventricular function. This improvement remains probable if an initial increased ejection fraction value resulting from raised catecholamines is taken into account. For the same reason the significant decrease of ejection fraction in group 2 might be overestimated. Our results are close to those of Rentrop *et al.*²² but differ from those of Reduto *et al.*¹⁰ who found a significantly increased ejection fraction after successful recanalisation on isotopic angiograms, despite a delayed intracoronary thrombolysis, up to 18 hours after the onset of symptoms, in his study. The different method of evaluating left ventricular function could explain this discrepancy.

The almost constant and sometimes striking improvement in the hypokinetic zone in group 1 reflects effective myocardial salvage. It cannot be because of a simple decrease in the systolic expansion of the infarcted zone since the hypokinetic zone deteriorated in the absence of recanalisation (group 2). This view is reinforced by isotopic studies,^{8 24 25} among them those of Maddahi *et al.*²⁶ who showed a simultaneous increase in left ventricular performance and thallium uptake in the reperfused zone.

In group 2, the deterioration in the hypokinesia led to a ventricular aneurysm in five out of eight patients as opposed to only one out of 15 patients in group 1, a significant difference ($p < 0.02$). The decrease in the contractility indices was higher in subgroup 2b than in subgroup 2a, which suggests a beneficial effect of even temporary recanalisation.

The delay between the onset of pain and intracoronary thrombolysis was longer in group 2 than in group

1. In the latter, however, no relation was found between this delay and the improvement in left ventricular function, in contrast to the findings of Rentrop *et al.*²²

If myocardial revascularisation cannot completely prevent infarction, our results show that early recanalisation leads to a notable degree of myocardial salvage, as previously shown in experimental studies.¹⁻³ The recanalisation seems to "freeze" the extension of the infarction and save the jeopardised myocardium from further and irreversible ischaemia. The absence of a relation between the delay and the left ventricular function changes may seem paradoxical, but the exact time at which the artery is occluded is not really known. In addition the collateral flow was not investigated in this study where the initial angiogram was limited to the infarct related coronary artery.

The small number of patients in the third study does not allow us to draw any conclusion as to the stability of the changes in regional left ventricular function variables observed at the second, except for the further decrease in ejection fraction in group 2. There was, however, a tendency towards an improvement of the hypokinesia in group 1 which could become significant with a few more patients.

If the improvement of regional left ventricular function after successful recanalisation confirms a partial salvage of jeopardised myocardium, the relatively small number of patients and the brief period of the survey do not allow us to draw conclusions on the effects of recanalisation on long term mortality and morbidity though there were no hospital deaths among the patients in whom recanalisation was successful and two among those in whom it was not. One must also bear in mind the remarkable reduction in hospital mortality in the German multicentre study which included over 200 patients.²⁰

Management following recanalisation is difficult when a severe stenosis persists, which is almost always the case. In this series, only three patients had an aortocoronary bypass performed to the recanalised artery after the second study. The decision to operate was only taken when there were multiple coronary lesions, when regional left ventricular function was satisfactory, and when the distal bed of the recanalised artery was of good quality. Merx *et al.*²⁰ reported an early reocclusion rate of 20%. In our study, the reocclusion rate was 26% at the second study. These figures suggest that after recanalisation coronary bypass should be undertaken whenever possible, as Mathey *et al.*²¹ have tried with good results. Alternatively immediate or delayed transluminal angioplasty might be attempted,^{21 27} though a better knowledge of the spontaneous evolution of residual coronary stenosis after recanalisation seems to be necessary in the light of our results. Further long term follow up

studies are needed.

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